US Army Medical Research and Materiel

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Marburg Virus Vaccines

This invention provides a method and a composition for use in inducing an immune response which is protective against infection with Marburg virus (MBGV) in nonhuman primates. Recombinant DNA constructs which comprise a Venezuelan equine encephalitis (VEE) replicon vector and at least one DNA fragment encoding a protective antigen from the Marburg virus are provided.

In the vaccine strategy, a gene coding for a protein of interest is cloned in place of the VEE virus structural genes; the result is a self-replicating RNA molecule that encodes its own replicase and transcriptase functions, and in addition makes abundant quantities of mRNA encoding the foreign protein. When the replicon RNA is transfected into eukaryotic cells, along with two helper RNAs that express the VEE structural proteins, the replicon RNA is packaged into VEE virus-like particles by the VEE virus structural proteins. Since the helper RNAs lack the packaging signals necessary for further propagation, the resulting VEE replicon particles (VRPs) are infectious for one cycle but are defective thereafter. Upon infection of an individual cell with a VRP, an abortive infection occurs in which the infected cell produces the protein of interest in abundance and is ultimately killed by the infection, but does not produce any viral progeny. As large quantities of the antigen are produced *in situ*, native processing of the antigens may evoke a broad array of immune responses.

MBGV was first recognized in 1967 when an outbreak of hemorrhagic fever occurred in humans in Europe, after the [illegible]tion of infected monkeys from Uganda. There were 31 cases of fever, of which 7 resulted in death. Concern about the virus is heightened by its known stability and infectivity in aerosol form. Thus, the identification of appropriate antigens and vaccine [illegible]es that can provide immunity to MBGV is needed.

Features and advantages:

- **Vaccination with glycoprotein (GP) expressed by VEE replicon completely protects nonhuman primates against MBGV**
- **Vaccination with GP, nucleo- protein (NP), or a virion structural protein (VP35) expressed by VEE replicon protects guinea pigs**
- **GP expressed by VEE replicon elicits more robust immunity than baculovirus-produced soluble GP**
- **VEE replicon produces large quantities of antigen *in situ***

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